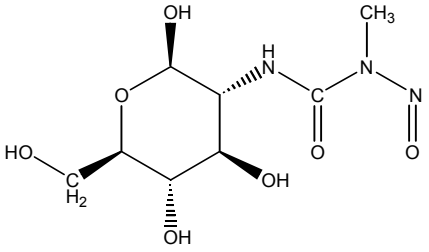
STREPTOZOTOCIN
CAS No. 18883-66-4
First Listed in the *Second Annual Report on Carcinogens*



CARCINOGENICITY

Streptozotocin is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC V.17, 1978; IARC S.4, 1982). When administered by intraperitoneal injection, streptozotocin induced increased incidences of kidney and lung tumors in mice of both sexes and produced uterine tumors in female mice. When administered by intraperitoneal injection, streptozotocin increased the incidences of kidney and pancreatic islet cell tumors in rats of both sexes, liver tumors in female rats, and peritoneal sarcomas in male rats. When administered by intraperitoneal injection, streptozotocin induced cholangiomas and hepatomas in hamsters. When administered as a single intravenous injection, streptozotocin induced kidney adenomas, adenocarcinomas, and sarcomas in rats of both sexes. Intravenous injection of streptozotocin induced hepatomas in hamsters.

There are no data available to evaluate the carcinogenicity of streptozotocin in humans (IARC V.4, 1974; IARC V.17, 1978).

PROPERTIES

Streptozotocin is a mixture of α- and ß-stereoisomers which occurs as pale yellow or off-white crystals, powder, or platelets. The research grade may be an off-white to tan solid. It is very soluble in water, ketones, and lower alcohols; slightly soluble in polar organic solvents; and insoluble in nonpolar organic solvents. The pure compound is sensitive to humidity and light. Streptozotocin decomposes to diazomethane in alkaline solutions at 0^{o} C. When heated to decomposition, it emits toxic fumes of nitrogen oxides (NO_x).

USE

Streptozotocin is an antibiotic originally derived from the soil micro-organism *Streptomyces achromogenes*. The principal therapeutic use for streptozotocin is in the treatment of metastasizing pancreatic islet cell tumors. It is also effective in treating malignant carcinoid tumors, especially of the small intestine. It has been investigated for use in diabetes, since it has specific toxic action on pancreatic ß-cells (IARC V.17, 1978). However, the compound has been shown to artificially induce diabetes in rats (Kirk-Othmer V.24, 1984). Streptozotocin has been shown to have a cytotoxic effect against several experimental tumors in animals. It may be of some value in combination regimens for pancreatic carcinoma and in secondary regimens for

Hodgkin's disease. Streptozotocin has been investigated as a potential antibacterial agent but has never been used commercially for this purpose (IARC V.17, 1978).

PRODUCTION

Streptozotocin is not used commercially. The USITC identified two domestic manufacturers of streptozotocin in 1987 and 1988, but no production volumes were reported (USITC, 1988, 1989). No current data on imports or exports of streptozotocin are available. Chem Sources reported a single domestic manufacturer of streptozotocin and 10 domestic suppliers (Chem Sources, 1986). Prior to 1983, there were two producers of streptozotocin identified by the USITC (USITC, 1983).

EXPOSURE

The primary routes of potential human exposure to streptozotocin are inhalation, injection, and dermal contact. The risk of potential exposure is greatest for patients actually receiving the drug. The usual adult dosage is 1-1.5 g/m^2 body surface injected intravenously or intra-arterially, weekly for 4 weeks, or 500 mg/m^2 daily for 5 days every six weeks (IARC V.17, 1978). Dosage reduction may be required in patients with renal insufficiency. Health professionals such as pharmacists, doctors, and nurses may be exposed while dispensing, preparing, or administering the pharmaceuticals. Potential occupational exposure occurs during streptozotocin production and during the formulation of the pharmaceuticals. However, this exposure is site limited. Streptozotocin is not active orally. The National Occupational Exposure Survey (1981-1983) indicated that 2,074 workers, including 1,714 women, potentially were exposed to streptozotocin (NIOSH, 1984). This estimate was derived from observations of the actual use of the compound (30% of total observations) and the use of tradename products known to contain the compound (70%).

REGULATIONS

EPA regulates streptozotocin under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) and the Resource Conservation and Recovery Act (RCRA). Under RCRA, it is regulated as a hazardous constituent of waste. A reportable quantity (RQ) of 1 lb has been established for releases of streptozotocin under CERCLA. FDA regulates streptozotocin as a prescription drug approved for treating metastatic islet cell carcinomas of the pancreas. OSHA regulates streptozotocin under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-134.